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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/011,167	10/05/1998	JOHANNES J. GEUZE	RILE.001.OOU	9536

31272 7590 10/19/2004

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/011,167	GEUZE ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,16 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,16 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a rule 371 continuation of PCT Serial Number PCT/NL96/00317.

Claims 1-12, 15 and 17 have been canceled.

New claims 18-20 have been added.

Claims 13, 14, 16 and 18-20 are currently pending and are the subject of examination in the present Office Action.

In view of Applicant's amendment filed July 26, 2004, the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 13, 14 and 16 stand rejected under 35 USC § 102(b) as being anticipated by Harding et al. (J. Immunology, 151:3988-3998, 1993, of record).

It was previously stated: "Harding teaches the subcellular fractionation of murine peritoneal macrophages to produce lysosomal fractions containing MHC Class II molecules (see entire article, especially page 3990, column 2, last 2 paragraphs in particular), and that fractions containing lysosomes and light density membranes contained peptide-MHC-II complexes that were detected by T cells, (see entire article especially page 3992, column 1, last paragraph in particular). Harding teaches the differential centrifugation of the membrane-containing fractions over a Percoll gradient at 100,000 x g, which is greater than the 70,000 x g recited in claims 14 and 16 and will pellet out all material obtainable at 70,000 x g. Harding teaches that B cells, another type of antigen presenting cell, comprise similar compartments (page 3997, second column in particular). The prior art teaching anticipates the claimed invention."

Applicant's arguments filed July 26, 2004 have been fully considered but they are not persuasive.

Applicant has amended the claims to recite that the vesicle is obtainable from the extracellular milieu of a B lymphocyte. Applicant argues that the amendment distinguishes the claimed vesicles from those of the prior art because Harding obtained vesicles by externalizing lysosomes. This position is not convincing in regard to the difference between the vesicles of the prior art and those of the instantly claimed invention. In fact, the instant specification appears to teach that the lysosomal vesicles taught by the prior art are the same as those instantly claimed. At page 2 the instant specification (as filed on October 31, 2000) recites:

> "most of the intracellular MHC class II molecules reside in a lysosome-like, MHC-class II-enriched compartment (MIIC) which contains characteristic membrane vesicles and concentrically arranged membrane sheets (...). MIICs and the related CIIVs (...), likely represent the meeting point between MHC class II and antigenic peptides (...). Once loaded with peptide, MHC class II molecules are transferred to the cell surface via an unknown pathway for presentation to T-lymphocytes."

This description is the same as the description of an "intermediate population" in the prior art relied in Applicant's citation on page 6 of the response. The instant specification further teaches that the membrane of these MIICs becomes contiguous with the cell membrane in an exocytotic fashion, bear the same surface markers as the lysosomes from which they arose and are secreted as exosomes into the external milieu (paragraph bridging pages 2-3). The last paragraph of page 7 of the instant specification equates the "exosomes" described on pages 2-3 with the "vesicles" of the claims and discloses that the "vesicles" are morphologically similar to the MIICs:

> "exosomes were isolated from the culture media of the human B cell line RN by differential centrifugation (Figure 2). Pelleted membranes were analyzed by SDS-PAGE and Western blotting. After removal of cells, the majority of MHC class II-containing membranes sediment at 70,000 x g (Figure 2A, lane 6). The 70,000 x g pellets were composed of a homogeneous population of vesicles labeled for MHC class II (Figure 2B). The vesicles were morphologically similar to those present in MIICs and in exocytotic profiles of sectioned cells."

Therefore, while the instantly disclosed method of isolating exosomal vesicles may be distinct from the method of isolating lysosomal vesicles taught in the prior art, there is no evidence that the vesicles themselves are any different, as they both present antigen to T cells in the context of MHC class II and, by admission of the instant specification, are morphologically similar. Therefore, absent a showing of a physical difference between the exosomal vesicles of the instantly claimed invention and the lysosomal vesicles taught in the prior art, the vesicles appear to be the same. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference between the materials, i.e., that the claims are directed to new materials and that such a difference would have been considered unexpected by one of ordinary skill in the art, that is, the claimed subject matter, if new, is unobvious. In the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

2. Claims 13 and 15 are rejected under 35 USC § 102(b) as being anticipated by Amigorena et al (Nature, 369:113-120, 1994, of record).

It was previously stated: "Amigorena teaches the subcellular fractionation of a B cell line to produce fractions containing membrane vesicles with MHC Class II molecules (see entire article, especially page 114, column 2, last paragraph in particular), which contained processed peptide (see entire article, especially page 118, first paragraph of the Discussion Section in particular). The prior art teaching anticipates the claimed invention."

Applicant again argues that the claimed invention is distinct from the teachings of the prior art because Amigorena teaches isolation of intracellular lysosomes representing an "intermediate" rather than exosomes from the external milieu. This argument is not persuasive for the same reasons set forth regarding Harding in section 1 supra.

The following new grounds of rejection have been necessitated by Applicant's amendment.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18 and 19 recite the limitation "isolated antigen" in line 1 of each claim, claim 18 recites the limitation twice. There is no antecedent basis for this limitation in the claim. Base claim 13 is drawn to and recites only an "isolated antigen presenting vesicle." There is no provision in the base claim for an independently claimed "isolated antigen." Note that if claims 18 and 19 are amended to recite "isolated antigen presenting vesicles" they will be subject to the same rejections under 35 USC § 102 as base claim 13, as the limitations of claims 18 and 19 would not render the compositions patentably distinct.

Claim 20 is ambiguous and unclear in the recitation of "culture media from B lymphocytes containing MHC class II protein" in lines 4-6. The claim is ambiguous as to whether the MHC class II protein is in the medium or in the B cells.

Claim 20 is further unclear as to whether the B cells are included in the centrifugation step or whether the culture medium is centrifuged without the cells.

Conclusion

5. No claim is allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
October 7, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
10/13/04